REMARKS

Status of the claims:

Claims 72-77, 81-89, 100 and 107-115 are pending.

Claim 116 is newly added and is supported by canceled claims 1-3, 5-7, 12-13, and 16-17, and by the description in the specification (e.g., page 6, lines 1-27; page 6, line 34 to page 7, line 2; Examples 1-4 on pages 22-27; etc.). No new matter has been added.

Claims 82 and 89 are withdrawn from consideration as drawn to non-elected species.

Invention:

Claims 72, 100 and 116 are the independent claims in this case. Claim 72 requires:

> 72. A conjugate comprising a synthetic polymer carrier comprising a minimum of 5 and a maximum of 100 monomeric units, the monomeric units comprising amino acids, the conjugate comprising 1-10 hapten molecules and 1-10 marker groups or solid phase binding groups, wherein the hapten molecules and the marker groups or solid phase binding groups are coupled to reactive side groups at predetermined positions on the polymeric carrier, such that distances between the hapten molecules an the marker groups or solid phase binding groups are defined thereby, and wherein the reactive side groups are amino groups and/or thiol groups.

Claim 100 is substantially identical to claim 72, except requires 2-10 hapten molecules. Claim 116 replaced the term "predetermined positions" with "a defined and reproducible distance."

Prior to the present invention, researchers typically produced peptide antigens using recombinant DNA techniques. After the peptide antigen was formed, marker groups were introduced randomly into the molecule. Because marker groups could not

be introduced at distinct positions on the antigen, variation in the immunoassays in which they were used occurred, decreasing the reliability of those immunoassays.

The present inventors were the first to link polypeptide antigens to marker groups at distinct positions in a reproducible manner. They used solid phase synthetic means and the resulting conjugate of the solid phase bead linked to the peptide antigen with haptens at defined and reproducible positions is new.

Declaration of Dr. Milan Mrksich:

Dr. Mrksich's qualifications are laid out in paragraphs 1 to 4 of the attached declaration. He is a person skilled in the art relevant to the claimed invention. Rather than copying large quotes from the declaration, the undersigned directs the examiner's attention to the relevant paragraphs of the declaration as noted.

35 USC § 112, First Paragraph:

Claims 72-77, 81, 83-88, 100 and 107-115 are rejected as failing to comply with the written description requirement. The test for whether this requirement is met is whether the claimed subject matter is described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. *Moba, B.V. v. Diamond Automation, Inc.*, 325 F.3d 1306, 1319, 66 USPQ2d 1429, 1438 (Fed. Cir. 2003).

The specification clearly conveys that applicants were in complete possession of (1) conjugates in which individual groups are incorporated in the carrier at defined and reproducible "predetermined positions" and (2) of conjugates containing "non-immunologically reactive" carriers.

"predetermined positions"

See Mrksich Declaration, paragraphs 10-12

The invention provides a strategy that can prepare structurally well-defined oligomeric molecules, wherein the positions of the haptens, labels and immobilization groups can be defined precisely. The specification refers to these sites as 'predetermined positions'. The method is based on using solid phase synthesis techniques to prepare linear oligomers—based on peptides, nucleic acids or peptide nucleic acids—that either incorporate the relevant groups at specified sites or that incorporate functional groups that permit a second reaction to introduce the groups at specified sites. Mrksich Declaration, ¶ 8. Dr. Mrksich describes some of the benefits of this approach in paragraph 9.

Dr. Mrksich testifies that:

> The Applicants unambiguously had possession of the "predetermined positions" element recited in the claims and, in my opinion, were in complete possession of conjugates wherein individual haptens, markers or immobilization groups are incorporated in the carrier at defined and reproducible "predetermined positions. Mrksich Declaration, ¶¶ 11.

Applicants have added new claim 116 as an alternate to the language of claims 72 and 100. In claim 116, the term "predetermined positions" is replaced with "a defined and reproducible distance."

"non-immunologically reactive" carriers

See Mrksich Declaration, paragraphs 13-15

The specification defines a non-immunologically reactive amino acid sequence as "an amino acid sequence which does not interfere with the test procedure in the intended application of the conjugate as an antigen in an immunological method of detection". Specification, page 16, lines 3-8. Dr. Mrksich testifies that "it is readily apparent to those skilled in the art that the carrier must not interact with antibodies in the solution. The Applicants were in possession of this element of the invention." Mrksich Declaration, ¶¶14-15.

In view of Dr. Mrksich's testimony that the inventors were in possession of the claimed invention at the time of filing, the present claims satisfy the written description requirment. Accordingly, withdrawal of this ground of rejection is respectfully requested.

35 USC § 112, Second Paragraph:

Claims 72-77, 81, 83-88, 100 and 107-115 are rejected as failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The test for whether this requirement is met is whether when a skilled artisan understands the metes and bounds of the claim and would understand how to avoid infringement. See *Morton Int'l, Inc. v. Cardinal Chem Co.,* 5 F.3d 1464, 1470, 28 USPQ2d 1190, 1195 (Fed. Cir. 1993).

"predetermined positions....defined thereby"

See Mrksich Declaration, paragraph 16

> The Applicants' description of the invention in these functional terms is accurate, efficient and the most informative for those skilled in the art. ...Further, a skilled artisan would understand how they could avoid infringing these claims. ... Mrksich Declaration, ¶ 16.

"non-immunologically reactive"

See Mrksich Declaration, paragraph 17

> Hence, it is not possible to detail structural limitations for each and every possible application, for the reasons described in paragraphs 13-15 of this declaration. The skilled artisan recognizes these issues, and will recognize the limitations of the claims that pertain to non-immunologically reactive carriers and understand how to avoid them. Mrksich Declaration, ¶ 17.

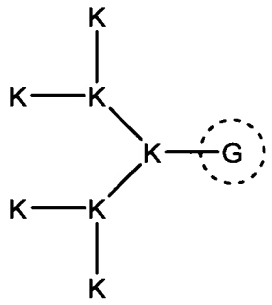
In view of Dr. Mrksich's testimony that a skilled artisan would both understand the claims and understand how to avoid them, the present claims are not indefinite. Accordingly, withdrawal of this ground of rejection is respectfully requested.

35 USC § § 102 and 103:

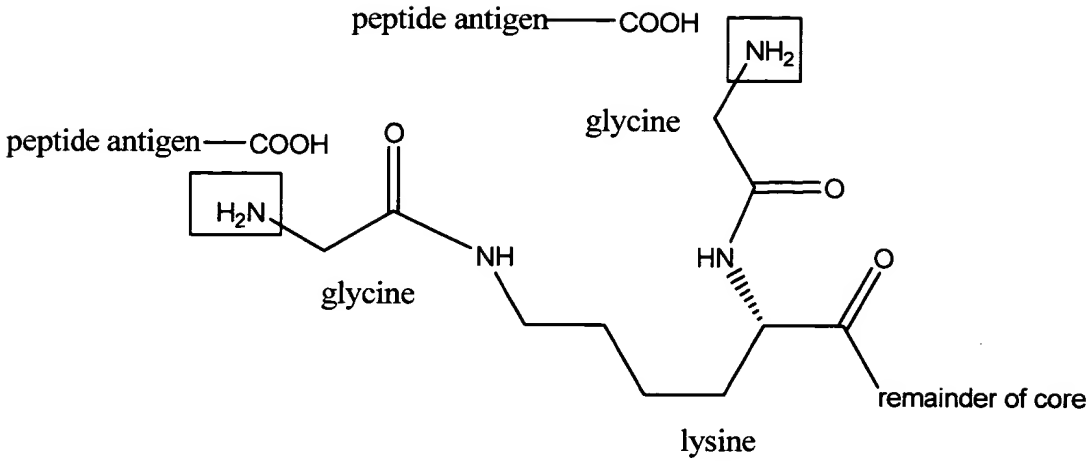
Claims 72, 74, 75, 86-88, 100, 107, 110, and 111 are rejected as anticipated by, or in the alternative obvious in view of, Tam (US 5,229,490).

Tam does not teach or suggest a carrier that simultaneously contains both a hapten molecule and a solid phase binding group, wherein the hapten molecule and the solid phase binding group are coupled to reactive amino and/or thiol side groups on the polymeric carrier (N.B., within the meaning of the claims, Applicants note that reactive amino side groups include both the N-terminus of a peptide as well as the individual amino side groups).

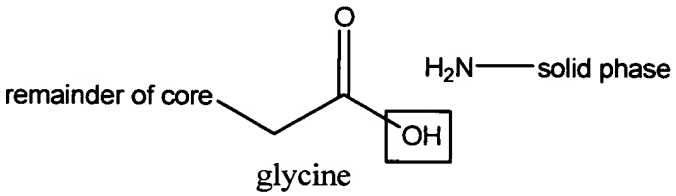
Tam instead has a polypeptide octabranched matrix core (K= lysine, G=Glycine).



Each lysine (K) is in turn linked to 2 glycines (G), such that 8 sites are available for attachment to a peptide antigen. Eight peptide antigens are linked to this core through the amino terminal groups of 8 glycine residues (see boxes below).



During synthesis, a solid phase is linked to the core via the glycine of the octabranched matrix core (see circled G above). The group linking the glycine to the solid phase is a hydroxyl group (see box below), not an amino group.



> The Applicants require that the haptens, markers and immobilization groups are bound through an amino or thiol group. In the Tam reference, the solid phase is bound to the carrier through a hydroxyl group. ... Hence, the Tam reference does not anticipate the invention claimed by the Applicants." Mrksich Declaration, ¶ 18.

Tam fails to meet each and every limitation of the claim. Further, no reference of record provides any indication of how to simultaneously introduce the haptens, marker groups or immobilization groups at predefined positions that are amino and thiol group. As such no *prima case* of obviousness has been established. For at least the reason set forth above, the claimed invention is neither anticipated by nor would have been

obvious in view of Tam. Accordingly, withdrawal of this ground of rejection is respectfully requested.

Claims 72, 74-76, 86-88, 100, 107, 110, and 111 are rejected as anticipated by, or in the alternative, obvious over Rose et al. (US 6,001,364). Rose et al. does not teach or suggest a carrier that contains hapten groups *and* either a marker or solid phase binding group coupled to reactive amino and/or thiol side groups on the polymeric carrier. Instead of two different groups, Rose et al. teach only a single group, haptens; and these groups are coupled via *oxime* groups, not amino and/or thiol groups.

> However, an important distinction between the method described in Rose and the method described by the Applicants is that the former teaches the preparation of a oligomeric molecule that is modified with only a single type of group, whereas the Applicants taught the preparation of an oligomeric molecule that contains the hapten at a set of predetermined positions and either a marker group or immobilization group at a set of predetermined positions. ... Hence, in my opinion, the reference of Rose does not anticipate the invention claimed by the Applicants." Mrksich Declaration, ¶ 19.

Rose fails to meet each and every limitation of the claim. No reference of record provides any indication of how to simultaneously introduce the haptens, marker groups or immobilization groups at predefined positions that are amino and thiol group. As such no *prima case* of obviousness has been established. For at least the reason set forth above, the claimed invention is neither anticipated by nor would have been obvious in view of Rose. Accordingly, withdrawal of this ground of rejection is respectfully requested.

SUMMARY

Applicants submit that pending Claims 72-77, 81-89, 100 and 107-115 are patentable. Applicant respectfully requests the Examiner grant early allowance of this application. The Examiner is invited to contact the undersigned attorneys for the Applicant via telephone if such communication would expedite this application.

Respectfully submitted,

S. Mrksich

K. Shannon Mrksich, Ph.D.
Registration No. 36,675
Attorney for Applicant

BRINKS HOFER GILSON & LIONE
P.O. BOX 10395
CHICAGO, ILLINOIS 60610
(312) 321-4283